AMENDMENTS TO THE CLAIMS

1. (Currently amended) A method for the quantification of real *in vivo* levels of low-level or unstable RNA from ~~a biological sample~~whole blood comprising the steps of:

(a) collecting ~~said biological sample~~the whole blood in a tube comprising a compound inhibiting RNA degradation and/or gene induction,

(b) forming a precipitate comprising nucleic acids;

(c) separating said precipitate of step (b) from the supernatant,

(d) dissolving said precipitate of step (c) using a buffer, forming a suspension,

(e) isolating nucleic acids from said suspension of step (d) using an automated device,

(f) dispersing/distributing a reagent mix for RT-PCR using an automated device,

(g) dispersing/distributing the nucleic acids isolated in step (e) within the dispersed reagent mix of step (f) using an automated device, and,

(h) determining the real *in vivo* levels of low-level or unstable RNA~~transcripts~~ using the nucleic acid/RT-PCR reagent mix of step (g) in an automated setup.

2. (Currently amended) The method according to claim 1, ~~whereby~~ wherein steps (a) and (b) are performed simultaneously.

3. (Currently amended) The method according to claim 1 ~~or 2~~, ~~whereby~~ wherein ~~said~~ the compound of step (a) comprises a quaternary amine surfactant.

4. (Currently amended) The method according to claim 3, ~~whereby~~ wherein said quaternary amine is tetradecyltrimethyl-ammonium oxalate.

5. (Canceled)

6. (Currently amended) The method according to claim 1 ~~or 2~~, ~~whereby said~~wherein the tube of step (a) is an open or a closed blood collecting tube.

7. (Currently amended) The method according to claim 1 ~~or 2~~, ~~whereby said~~wherein the buffer of step (d) is a guanidine-thiocyanate-containing buffer.

8. (Canceled)

9. (Currently amended) The method according to claim 1~~or 2~~, ~~whereby said~~wherein the isolation of nucleic acids of step (e) is performed using RNA-capturing beads.

10. (Canceled)

11. (Currently amended) The method according to claim 1~~or 2~~, ~~whereby~~wherein said *in vivo* levels are determined using real time PCR.

12. (Currently amended) The method according to claim 1~~or 2~~, ~~whereby~~wherein said quantification is performed using a ~~biological~~ whole blood sample of 100 µl.

13-17. (Canceled)

18. (Currently amended) A method for the quantification of low-level or unstable DNA from ~~a biological sample~~whole blood wherein a method is used as performed for the quantification of RNA according to the method of claim 1, wherein the RT reaction is skipped and wherein the compound of step (a) also protects the DNA from being degraded.

19. (Canceled)

20. (Currently amended) A method for the monitoring/detection of changes of real *in vivo* low-level or unstable nucleic acids levels in a biological agent present in ~~a biological sample~~whole blood according to claim 1.

21. (Currently amended) The method according to claim 20 ~~whereby~~ wherein said biological agent is selected from the group consisting of eukaryotic cells, prokaryotic cells, viruses and phages.

22. (Currently amended) A method for the monitoring/detection of changes of real *in vivo* low-level or unstable nucleic acids of a biological agent in ~~a biological sample~~whole blood, in order to diagnose a certain disease according to claim 1.

23. (Currently amended) A method for the monitoring/detection of changes of real *in vivo* low-level or unstable nucleic acids of a biological agent in ~~a biological sample~~whole blood, in order to screen for a compound for the production of a medicament for curing a disease according to claim 1.

24. (Canceled)

25. (Currently amended) The method according to claim 22~~or 23~~, wherein said disease is an immuno-related disease.

26. (Previously presented) The method according to claim 23, for the detection/monitoring/screening of a compound, wherein said compound is an immunomodulatory compound which may be selected from the group consisting of eukaryotic cells, prokaryotic cells, viruses, phages, parasites, drugs (natural extracts, organic molecule, peptide, proteins, nucleic acids), medical treatment, vaccine and transplants.

27. (Currently amended) A method for the detection/monitoring of real *in vivo* levels of low-level or unstable epitope specific CTLs or immuno-related transcripts according to claim 1.

28. (Currently amended) A method to identify an agent capable of modifying the immunological status of a subject via the analysis of real *in vivo* levels of low-level or unstable epitope specific CTLs comprising the steps of:

(a) applying an immunomodulatory agent(s) into a subject,

(b) sampling whole blood from said subject,

(c) optionally, pulsing blood cells present in the whole blood sample of step (b) with an identical/similar and/or different immunomodulatory agent as applied in step (a),

(d) collecting pulsed blood cells of step (c) or non-pulsed blood cells of step (b) in a tube comprising a compound inhibiting RNA degradation and/or gene induction, or adding said compound to the pulsed/non-pulsed cells,

(e) forming a precipitate comprising nucleic acids,

(f) separating said precipitate of step (e) from the supernatant,

(g) dissolving said precipitate of step (f) using a buffer, forming a suspension,

(h) isolating nucleic acids from said suspension of step (g) using an automated device,

(i) dispersing/distributing a reagent mix for RT-PCR using an automated device,

(j) dispersing/distributing the nucleic acids isolated in step (h) within the dispersed reagent mix of step (i) using an automated device,

(k) detecting/monitoring/analyzing the real *in vivo* levels of low-level or unstable epitope specific CTLs-related transcripts in the dispersed solution of step (j) in an automated setup, and,

(l) identifying agents able to modify the immunological status of said subject, whereby, in case the agent of step (a) is already present in the subject, step (a) is omitted.

29. (Currently amended) A method to identify an agent capable of modifying the immunological status of a subject:

(a) applying an immunomodulatory agent(s) into a subject,

(b) sampling whole blood from said subject,

(c) optionally, pulsing blood cells present in the whole blood sample of step (b) with an identical/similar and/or different immunomodulatory agent as applied in step(a),

(d) collecting pulsed blood cells of step (c) or non-pulsed blood cells of step (b) in a tube comprising a compound inhibiting RNA degradation and/or gene induction, or adding said compound to the pulsed/non-pulsed cells,

(e) forming a precipitate comprising nucleic acids,

(f) separating said precipitate of step (e) from the supernatant,

(g) dissolving said precipitate of step (f) using a buffer, forming a suspension,

(h) isolating nucleic acids from said suspension of step (g) using an automated device,

(i) dispersing/distributing a reagent mix for RT-PCR using an automated device,

(j) dispersing/distributing the nucleic acids isolated in step (h) within the dispersed reagent mix of step (i) using an automated device,

(k) detecting/monitoring/analyzing the real *in vivo* levels of low-level or unstable immuno-related transcripts in the dispersed solution of step (j) in an automated setup, and,

(l) identifying agents able to modify the immunological status of said subject, whereby, in case the agent of step (a) is already present in the subject, step (a) is omitted.

30. (Currently amended) A method for the diagnosis/prognosis/monitoring of a clinical status affecting the immune system in a subject comprising the steps of:

(a) sampling whole blood from said subject in a tube comprising a compound inhibiting RNA degradation and/or gene induction, or adding said compound to the blood cells,

(b) forming a precipitate comprising nucleic acids,

(c) separating said precipitate of step (b) from the supernatant,

(d) dissolving said precipitate of step (c) using a buffer, forming a suspension,

(e) isolating nucleic acids from said suspension of step (d) using an automated device,

(f) dispersing/distributing a reagent mix for RT-PCR using an automated device,

(g) dispersing/distributing the nucleic acids isolated in step (e) within the dispersed reagent mix of step (f) using an automated device,

(h) detecting/monitoring/analyzing the *in vivo* levels of low-level or unstable immuno-related transcripts in the dispersed solution of step (g) in an automated setup, and,

(i) detecting/monitoring the change in real *in vivo* levels of low-level or unstable immuno-related transcripts, and

(j) diagnosing/prognosing/monitoring the disease affecting the immune system.

31. (Currently amended) A method for the diagnosis/prognosis/monitoring of a clinical status affecting the immune system in a subject comprising the steps of:

(a) sampling whole blood from said subject,

(b) pulsing blood cells present in the whole blood sample of step (a) with an identical/similar and/or different immunomodulatory agent as present in the subject,

(c) collecting pulsed blood cells of step (b) in a tube comprising a compound inhibiting RNA degradation and/or gene induction, or adding said compound to the pulsed cells,

(d) forming a precipitate comprising nucleic acids,

(e) separating said precipitate of step (d) from the supernatant,

(f) dissolving said precipitate of step (e) using a buffer, forming a suspension,

(g) isolating nucleic acids from said suspension of step (f) using an automated device,

(h) dispersing/distributing a reagent mix for RT-PCR using an automated device,

(i) dispersing/distributing the nucleic acids isolated in step (g) within the dispersed reagent mix of step (h) using an automated device,

(j) detecting/monitoring/analyzing the real *in vivo* levels of low-level or unstable immuno-related transcripts in the dispersed solution of step (i) in an automated setup,

(k) detecting/monitoring the change in *in vivo* levels of immuno-related transcripts, and,

(l) diagnosing/prognosing/monitoring the disease affecting the immune system.

32. (Currently amended) The method according to ~~any of claims 25 to 31~~claim 25, wherein the immuno-related disease is selected from the group consisting of autoimmunity, rheumatoid arthritis, multiple sclerosis, cancer (eg. in cancer immunotherapy), immunodeficiencies (eg. in AIDS), allergy, graft rejection and Graft versus Host Disease (GVHD) (eg. in transplantation), wherein the immunomodulatory compound or agent influences one of said diseases; or wherein the change of the immuno-related transcripts or the epitope specific CTLs-related or T Helper lymphocyte-related transcripts indicate the presence of one of said diseases~~; or wherein the immunological status illustrates the status of one of said diseases~~.

33. (Previously presented) The method according to claim 32, wherein said immuno-related transcript is selected from the group consisting of nucleic acids coding for chemokine, cytokine, growth factors, cytotoxic markers, transcription factors, members of the TNF-related cytokine-receptor superfamily and their ligands, apoptosis markers, immunoglobulins, T-cell receptor, and any marker related to the activation or the inhibition of the immune system known or to be discovered.

34. (Previously presented) The method according to claim 33, wherein said nucleic acid codes for a marker selected from the group consisting of IL-1ra, IL-1β, IL-2, IL-4, IL-5, IL-9, IL-10, IL-12p35, IL-12p40, IL-13, TNF-α, IFN-γ, IFN-α, TGF-β, and any interleukin or cytokine involved or not in the immune response.

35. (Previously presented) The method according to claim 32, wherein said epitope specific CTLs-related or T Helper lymphocyte-related transcript is selected from the group consisting of nucleic acids coding for cytokines, cytokine receptors, cytotoxines, inflammatory or anti-inflammatory mediators, members of the TNF-related cytokine-receptor superfamily and their ligands, G-protein coupled receptors and their ligands, tyrosine kinase receptors and their ligands, transcription factors, and proteins involved in intra-cellular signaling pathways.

36. (Previously presented) The method according to claim 35, wherein said nucleic acid codes for a marker selected from the group consisting of granzyme, perforines, prostaglandins, leukotrienes, immunoglobulin and immunoglobulin superfamily receptors, Fas and Fas ligand, T cell receptor, chemokine and chemokine receptors, protein-tyrosine kinase C, protein-tyrosine kinase A, Signal Transducer and Activator of Transcription (STAT), NF-kB, T-bet, GATA-3, and Oct-2.

37-39. (Canceled)

40. (New) The method according to claim 23, wherein said disease is an immuno-related disease.

41. (New) The method according to claim 40, wherein the immuno-related disease is selected from the group consisting of autoimmunity, rheumatoid arthritis, multiple sclerosis, cancer (eg. in cancer immunotherapy), immunodeficiencies (eg. in AIDS), allergy, graft rejection and Graft versus Host Disease (GVHD) (eg. in transplantation), wherein the immunomodulatory compound or agent influences one of said diseases; or wherein the change of the immuno-related transcripts

or the epitope specific CTLs-related or T Helper lymphocyte-related transcripts indicate the presence of one of said diseases.

42. (New) The method according to claim 41, wherein said immuno-related transcript is selected from the group consisting of nucleic acids coding for chemokine, cytokine, growth factors, cytotoxic markers, transcription factors, members of the TNF-related cytokine-receptor superfamily and their ligands, apoptosis markers, immunoglobulins, T-cell receptor, and any marker related to the activation or the inhibition of the immune system known or to be discovered.

43. (New) The method according to claim 42, wherein said nucleic acid codes for a marker selected from the group consisting of IL-1ra, IL-1 , IL-2, IL-4, IL-5, IL-9, IL-10, IL-12p35, IL-12p40, IL-13, TNF-[alpha], IFN-[gamma], IFN-[alpha], TGF-[beta], and any interleukin or cytokine involved or not in the immune response.

44. (New) The method according to claim 41, wherein said epitope specific CTLs-related or T Helper lymphocyte-related transcript is selected from the group consisting of nucleic acids coding for cytokines, cytokine receptors, cytotoxines, inflammatory or anti-inflammatory mediators, members of the TNF-related cytokine-receptor superfamily and their ligands, G-protein coupled receptors and their ligands, tyrosine kinase receptors and their ligands, transcription factors, and proteins involved in intra-cellular signaling pathways.

45. (New) The method according to claim 44, wherein said nucleic acid codes for a marker selected from the group consisting of granzyme, perforines, prostaglandins, leukotrienes, immunoglobulin and immunoglobulin superfamily receptors, Fas and Fas ligand, T cell receptor, chemokine and chemokine receptors, protein-tyrosine kinase C, protein-tyrosine kinase A, Signal Transducer and Activator of Transcription (STAT), NF-kB, T-bet, GATA-3, and Oct-2.

46. (New) The method according to claim 28, wherein the immunological status illustrates the status of a immuno-related disease selected from the group consisting of autoimmunity,

rheumatoid arthritis, multiple sclerosis, cancer (eg. in cancer immunotherapy), immunodeficiencies (eg. in AIDS), allergy, graft rejection and Graft versus Host Disease (GVHD) (eg. in transplantation), wherein the immunomodulatory compound or agent influences one of said diseases; or wherein the change of the immuno-related transcripts or the epitope specific CTLs-related or T Helper lymphocyte-related transcripts indicate the presence of one of said diseases.

47. (New) The method according to claim 46, wherein said immuno-related transcript is selected from the group consisting of nucleic acids coding for chemokine, cytokine, growth factors, cytotoxic markers, transcription factors, members of the TNF-related cytokine-receptor superfamily and their ligands, apoptosis markers, immunoglobulins, T-cell receptor, and any marker related to the activation or the inhibition of the immune system known or to be discovered.

48. (New) The method according to claim 47, wherein said nucleic acid codes for a marker selected from the group consisting of IL-1ra, IL-1 , IL-2, IL-4, IL-5, IL-9, IL-10, IL-12p35, IL-12p40, IL-13, TNF-[alpha], IFN-[gamma], IFN-[alpha], TGF-[beta], and any interleukin or cytokine involved or not in the immune response.

49. (New) The method according to claim 46, wherein said epitope specific CTLs-related or T Helper lymphocyte-related transcript is selected from the group consisting of nucleic acids coding for cytokines, cytokine receptors, cytotoxines, inflammatory or anti-inflammatory mediators, members of the TNF-related cytokine-receptor superfamily and their ligands, G-protein coupled receptors and their ligands, tyrosine kinase receptors and their ligands, transcription factors, and proteins involved in intra-cellular signaling pathways.

50. (New) The method according to claim 49, wherein said nucleic acid codes for a marker selected from the group consisting of granzyme, perforines, prostaglandins, leukotrienes, immunoglobulin and immunoglobulin superfamily receptors, Fas and Fas ligand, T cell receptor, chemokine and chemokine receptors, protein-tyrosine kinase C, protein-tyrosine kinase A, Signal

Transducer and Activator of Transcription (STAT), NF-kB, T-bet, GATA-3, and Oct-2.

51. (New) The method according to claim 29, wherein the immunological status illustrates the status of a immuno-related disease selected from the group consisting of autoimmunity, rheumatoid arthritis, multiple sclerosis, cancer (eg. in cancer immunotherapy), immunodeficiencies (eg. in AIDS), allergy, graft rejection and Graft versus Host Disease (GVHD) (eg. in transplantation), wherein the immunomodulatory compound or agent influences one of said diseases; or wherein the change of the immuno-related transcripts or the epitope specific CTLs-related or T Helper lymphocyte-related transcripts indicate the presence of one of said diseases.

52. (New) The method according to claim 51, wherein said immuno-related transcript is selected from the group consisting of nucleic acids coding for chemokine, cytokine, growth factors, cytotoxic markers, transcription factors, members of the TNF-related cytokine-receptor superfamily and their ligands, apoptosis markers, immunoglobulins, T-cell receptor, and any marker related to the activation or the inhibition of the immune system known or to be discovered.

53. (New) The method according to claim 52, wherein said nucleic acid codes for a marker selected from the group consisting of IL-1ra, IL-1 , IL-2, IL-4, IL-5, IL-9, IL-10, IL-12p35, IL-12p40, IL-13, TNF-[alpha], IFN-[gamma], IFN-[alpha], TGF-[beta], and any interleukin or cytokine involved or not in the immune response.

54. (New) The method according to claim 51, wherein said epitope specific CTLs-related or T Helper lymphocyte-related transcript is selected from the group consisting of nucleic acids coding for cytokines, cytokine receptors, cytotoxines, inflammatory or anti-inflammatory mediators, members of the TNF-related cytokine-receptor superfamily and their ligands, G-protein coupled receptors and their ligands, tyrosine kinase receptors and their ligands, transcription factors, and proteins involved in intra-cellular signaling pathways.

55. (New) The method according to claim 54, wherein said nucleic acid codes for a marker selected from the group consisting of granzyme, perforines, prostaglandins, leukotrienes, immunoglobulin and immunoglobulin superfamily receptors, Fas and Fas ligand, T cell receptor, chemokine and chemokine receptors, protein-tyrosine kinase C, protein-tyrosine kinase A, Signal Transducer and Activator of Transcription (STAT), NF-kB, T-bet, GATA-3, and Oct-2.

56. (New) The method according to claim 30, wherein the immunological status illustrates the status of a immuno-related disease selected from the group consisting of autoimmunity, rheumatoid arthritis, multiple sclerosis, cancer (eg. in cancer immunotherapy), immunodeficiencies (eg. in AIDS), allergy, graft rejection and Graft versus Host Disease (GVHD) (eg. in transplantation), wherein the immunomodulatory compound or agent influences one of said diseases; or wherein the change of the immuno-related transcripts or the epitope specific CTLs-related or T Helper lymphocyte-related transcripts indicate the presence of one of said diseases.

57. (New) The method according to claim 56, wherein said immuno-related transcript is selected from the group consisting of nucleic acids coding for chemokine, cytokine, growth factors, cytotoxic markers, transcription factors, members of the TNF-related cytokine-receptor superfamily and their ligands, apoptosis markers, immunoglobulins, T-cell receptor, and any marker related to the activation or the inhibition of the immune system known or to be discovered.

58. (New) The method according to claim 57, wherein said nucleic acid codes for a marker selected from the group consisting of IL-1ra, IL-1 , IL-2, IL-4, IL-5, IL-9, IL-10, IL-12p35, IL-12p40, IL-13, TNF-[alpha], IFN-[gamma], IFN-[alpha], TGF-[beta], and any interleukin or cytokine involved or not in the immune response.

59. (New) The method according to claim 56, wherein said epitope specific CTLs-related or T Helper lymphocyte-related transcript is selected from the group consisting of nucleic acids coding for cytokines, cytokine receptors, cytotoxines, inflammatory or anti-inflammatory

mediators, members of the TNF-related cytokine-receptor superfamily and their ligands, G-protein coupled receptors and their ligands, tyrosine kinase receptors and their ligands, transcription factors, and proteins involved in intra-cellular signaling pathways.

60. (New) The method according to claim 59, wherein said nucleic acid codes for a marker selected from the group consisting of granzyme, perforines, prostaglandins, leukotrienes, immunoglobulin and immunoglobulin superfamily receptors, Fas and Fas ligand, T cell receptor, chemokine and chemokine receptors, protein-tyrosine kinase C, protein-tyrosine kinase A, Signal Transducer and Activator of Transcription (STAT), NF-kB, T-bet, GATA-3, and Oct-2.

61. (New) The method according to claim 31, wherein the immunological status illustrates the status of a immuno-related disease selected from the group consisting of autoimmunity, rheumatoid arthritis, multiple sclerosis, cancer (eg. in cancer immunotherapy), immunodeficiencies (eg. in AIDS), allergy, graft rejection and Graft versus Host Disease (GVHD) (eg. in transplantation), wherein the immunomodulatory compound or agent influences one of said diseases; or wherein the change of the immuno-related transcripts or the epitope specific CTLs-related or T Helper lymphocyte-related transcripts indicate the presence of one of said diseases.

62. (New) The method according to claim 61, wherein said immuno-related transcript is selected from the group consisting of nucleic acids coding for chemokine, cytokine, growth factors, cytotoxic markers, transcription factors, members of the TNF-related cytokine-receptor superfamily and their ligands, apoptosis markers, immunoglobulins, T-cell receptor, and any marker related to the activation or the inhibition of the immune system known or to be discovered.

63. (New) The method according to claim 62, wherein said nucleic acid codes for a marker selected from the group consisting of IL-1ra, IL-1 , IL-2, IL-4, IL-5, IL-9, IL-10, IL-12p35, IL-12p40, IL-13, TNF-[alpha], IFN-[gamma], IFN-[alpha], TGF-[beta], and any interleukin or cytokine involved or not in the immune response.

64. (New) The method according to claim 61, wherein said epitope specific CTLs-related or T Helper lymphocyte-related transcript is selected from the group consisting of nucleic acids coding for cytokines, cytokine receptors, cytotoxines, inflammatory or anti-inflammatory mediators, members of the TNF-related cytokine-receptor superfamily and their ligands, G-protein coupled receptors and their ligands, tyrosine kinase receptors and their ligands, transcription factors, and proteins involved in intra-cellular signaling pathways.

65. (New) The method according to claim 64, wherein said nucleic acid codes for a marker selected from the group consisting of granzyme, perforines, prostaglandins, leukotrienes, immunoglobulin and immunoglobulin superfamily receptors, Fas and Fas ligand, T cell receptor, chemokine and chemokine receptors, protein-tyrosine kinase C, protein-tyrosine kinase A, Signal Transducer and Activator of Transcription (STAT), NF-kB, T-bet, GATA-3, and Oct-2.

66. (New) The method according to claim 1 or 2, wherein said quantification is performed using a whole blood sample of 20-200 µl.